Differences in presentation and clinical outcomes between left or right bundle branch block and ST segment elevation in patients with acute myocardial infarction

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Abstract: <jats:sec>Background: In patients with acute myocardial infarction, the presence of a left bundle branch block or right bundle branch block may be associated with worse prognosis compared to isolated ST segment elevation. However, specificities in clinical presentation and outcomes of acute myocardial infarction patients with left bundle branch block or right bundle branch block are poorly characterized. </jats:sec><jats:sec>Methods: We analysed acute myocardial infarction patients with left bundle branch block (n=880), right bundle branch block (n=732) or ST segment elevation without bundle branch block (n=15,852) included in the Acute Myocardial Infarction in Switzerland-Plus registry between 2008–2019. </jats:sec><jats:sec>Results: Acute myocardial infarction patients with bundle branch block were older and had more pre-existing cardiovascular conditions compared to ST segment elevation. Pulmonary oedema and cardiogenic shock were most frequent in patients with left bundle branch block (18.8% vs 12.0% for right bundle branch block and 7.9% for ST segment elevation, plt;0.001). Acute myocardial infarction patients with bundle branch block had more three-vessel (40.6% vs 25.3%, plt;0.001 vs ST segment elevation) and left main disease (5.6% vs 2.0%, plt;0.001 vs ST segment elevation). Major adverse cardiac and cerebrovascular events, a composite of reinfarction, stroke/transient ischaemic attack, and death during hospitalization, were highest in acute myocardial infarction patients with left bundle branch block (13.9% vs 9.9% for right bundle branch block and 6.7% for ST segment elevation, plt;0.05), which was driven by hospital mortality. After multivariate adjustment, however, mortality was similar in patients with left bundle branch block and lower in patients with right bundle branch block, respectively, when compared to ST segment elevation. Mortality was only increased when a right bundle branch block with concomitant STE was present (odds ratio 1.77, 95% confidence interval 1.19–2.64, plt;0.01 vs ST segment elevation). </jats:sec><jats:sec>Conclusions: Compared to ST segment elevation, an isolated bundle branch block reflects high-risk clinical characteristics but does not independently determine increased hospital mortality in acute myocardial infarction. </jats:sec>

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Differences in presentation and clinical outcomes between left or right bundle branch block and ST segment elevation in patients with acute myocardial infarction

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Abstract

Background: In patients with acute myocardial infarction (AMI), the presence of a left bundle branch block (LBBB) or right bundle branch block (RBBB) may be associated with worse prognosis compared to isolated ST segment elevation (STE). However, specificities in clinical presentation and outcomes of AMI patients with LBBB or RBBB are poorly characterized.

Methods: We analyzed AMI patients with LBBB (*n*=880), RBBB (*n*=732) or STE without bundle branch block (BBB, *n*=15'852) included in the Acute Myocardial Infarction in Switzerland (AMIS)-Plus registry between 2008 and 2019.

Results: AMI patients with BBB were older and had more preexisting cardiovascular conditions compared to STE. Pulmonary edema and cardiogenic shock were most frequent in patients with LBBB (18.8% vs. 12.0% for RBBB and 7.9% for STE, $p<0.001$). AMI patients with BBB had more three-vessel (40.6% vs. 25.3%, $p<0.001$ vs. STE) and left main disease (5.6% vs. 2.0%, $p<0.001$ vs. STE). Major adverse cardiac and cerebrovascular events, a composite of reinfarction, stroke/transient ischemic attack, and death during hospitalization, were highest in AMI patients with LBBB (13.9% vs. 9.9% for RBBB and 6.7% for STE, $p<0.05$), which was driven by hospital mortality. After multivariate adjustment, however, mortality was similar in patients with LBBB and reduced in patients with RBBB, respectively, when compared to STE. Mortality was only increased when an RBBB with concomitant STE was present (OR 1.77, 95% CI 1.19-2.64, $p<0.01$ vs. STE).

Conclusions: Compared to STE, an isolated BBB reflects high-risk clinical characteristics but does not independently determine increased hospital mortality in AMI.

Keywords: Acute coronary syndrome; ECG; left bundle branch block; myocardial infarction; right bundle branch block; STEMI.

Introduction

In patients with suspected acute myocardial infarction (AMI), a 12-lead electrocardiogram (ECG) must be acquired and interpreted within 10 minutes of first medical contact.[1, 2] In the context of a suggestive clinical presentation, ST segment elevation (STE) frequently indicates an acute occlusion of a coronary artery.[1, 2] In this setting, a new or presumably new left bundle branch block (LBBB) or right bundle branch block (RBBB) may reflect a large territory of acute ischemia involving the proximal conducting system or diffusely damaging the ventricular myocardium leading to delayed conduction, while at the same time due to the bundle branch block (BBB) the STE may be concealed.[3] Therefore, European Society of Cardiology (ESC) guidelines not only recommend urgent coronary angiography in AMI patients with STE, but likewise also with a (presumably) new LBBB or RBBB and signs or symptoms of ongoing myocardial ischemia.[2] This treatment recommendation is based on retrospective analyses and on the fact that the ECG, the cornerstone of diagnosis, is frequently not interpretable. However, patients with suspected AMI and LBBB or RBBB represent a much more heterogeneous population with a lower probability of an occluded culprit artery compared to patients with isolated STE.[3]

Specificities in clinical presentation and outcomes of AMI patients with LBBB or RBBB have been poorly characterized, and previous studies have yielded conflicting results regarding the prognostic significance of an LBBB or RBBB in this setting. In contrast to a preexisting BBB, a new or presumably new, persistent LBBB or RBBB in patients with AMI was found to be an independent predictor of short- or long-term mortality in most,[4-15] but not in all studies.[16, 17] In addition, while some authors reported increased mortality in AMI patients presenting with an LBBB compared with an RBBB,[5, 13] others found the opposite[4, 8, 14, 15] or no difference.[7, 9, 10, 16] However, many previous studies were hampered by relatively low patient numbers, dated back

to the fibrinolytic era when coronary angiography and coronary revascularization were not routinely performed, or represented post hoc analyses of randomized trials. We therefore addressed specificities of clinical presentation and outcomes in AMI patients with LBBB or RBBB and compared them with the isolated STE population in a large, contemporary, nationwide cohort of unselected AMI patients.

Methods

Acute Myocardial Infarction in Switzerland (AMIS)-Plus registry

The AMIS-Plus registry was initiated in 1997 and collects data from patients admitted with an acute coronary syndrome to one of 84 contributing Swiss hospitals, ranging from community hospitals to large tertiary care facilities, as described previously.[18] Anonymized data are provided by the treating physician or a trained study nurse via electronic or paper-based forms, and checked for completeness, plausibility and consistency by the AMIS-Plus data center (Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Switzerland). Data acquisition and analysis are performed in accordance with good clinical practice guidelines, undergo regular external auditing, and have been approved by the supra-regional and cantonal ethics committees of all participating hospitals. The ethics committees waived the requirement to obtain patients' informed consent.

Study population and outcomes

This investigation analyzed data from AMI patients enrolled in the AMIS-Plus registry between January 2008 and June 2019 with either an LBBB, RBBB, or STE in the ECG on admission. A final diagnosis of AMI required the detection of a rise and/or fall in cardiac troponin I or T values, with at least one value above the 99th percentile upper reference limit.[19-21] If troponin assays were unavailable, an increase in creatine kinase myocardial band (CK-MB) level ≥2-fold above the upper reference limit was accepted. The choice of the cardiac biomarker assay used was at the discretion of the contributing hospital. In addition, clinical evidence of acute myocardial ischemia including typical symptoms or new ischemic ECG changes were required.[19-21] LBBB and RBBB were considered new or presumably new by the treating physician, and STE was defined as described.[19-21] Patient comorbidities were assessed based on

the Charlson index.[22] A >50% stenosis in the coronary angiogram was considered significant as diagnosed by the treating interventional cardiologist.

As primary outcome, we analyzed major adverse cardiac and cerebrovascular events (MACCE), representing a composite of reinfarction, stroke/transient ischemic attack (TIA), and/or death during hospitalization. Secondary outcomes included the individual components of the primary outcome, as well as cardiogenic shock and acute renal failure during hospitalization. Reinfarction was defined as the presence of recurrent ischemic symptoms or clinical signs following the initial MI, with at least a 20% increase in cardiac biomarkers during repeated sampling. Stroke and TIA were defined as the presence of a new focal neurologic deficit thought to be of vascular origin, with signs or symptoms lasting more or less than 24 h, respectively. Cardiogenic shock was diagnosed when hypotension (systolic blood pressure <90mmHg) despite adequate filling status was associated with evidence of hypoperfusion, and acute renal failure was defined as described.[23]

Statistical analyses

Demographic and clinical characteristics, therapeutic strategies and hospital outcomes were analyzed stratified according to the findings in the initial ECG. Normally distributed data were analyzed using the unpaired Student's *t* test and given as mean ± standard deviation (SD). Non-normally distributed data were analyzed using the nonparametric Mann-Whitney *U* test and given as median and interquartile range (IQR). Categorical data were analyzed by the Fisher's exact or the Pearson χ^2 test, as appropriate. To study the association of BBBs with hospital mortality, multivariate logistic regression modeling using the following covariates was performed: isolated LBBB, isolated RBBB, isolated STE, combined LBBB and STE, combined RBBB and STE, age, female sex, resuscitation prior to admission, Killip class ≥3, Charlson comorbidity index, performance of PCI, as well as heart rate, systolic blood pressure, and creatinine values. Results are given as odds ratios (OR)

with 95% confidence intervals (CI). All analyses were performed using IBM SPSS Statistics software (version 24, IBM Corp., Armonk, NY). Two-sided *P* values <0.05 were considered significant.

Results

Patient characteristics

Between January 1st 2008 and June 30th 2019, 33'157 AMI patients were included in the AMIS-Plus registry. Of these, 15'291 patients (46%) without STE or a BBB and 402 patients (1.2%) with missing ECG data were excluded from the analysis. Among the remaining cohort of patients (*n*=17'464), 880 (5.0%) had an LBBB, 732 (4.2%) had an RBBB, and 15'852 (90.8%) had isolated STE in the initial ECG, and these three groups were compared in the current investigation. Baseline characteristics are shown in **Table 1**. Compared to the group with RBBB, AMI patients with an LBBB were older and had a higher percentage of women. Patients with LBBB also more frequently had hypertension, coronary artery disease, heart failure, and kidney disease (all $p<0.05$ *vs.* RBBB). Compared to isolated STE, AMI patients with LBBB or RBBB were ~10 years older and had more comorbidities, including a higher prevalence of preexisting cardiovascular and renal conditions.

	LBBB (*n*=880)	RBBB (*n*=732)	STE (*n*=15'852)	*P* value (LBBB vs. RBBB)	*P* value (BBB vs. STE)
Demographic characteristics					
Age (years), mean±SD	75.6±10.3	73.1±11.4	64.2±13.0	<0.001	<0.001
Sex (female), % (*n*/N)	32.7 (288/880)	16.8 (123/732)	25.9 (3'961/15'852)	<0.001	<0.001
Medical history, % (*n*/N)					
Hypertension	83.6 (694/830)	76.3 (530/695)	56.8 (8'428/14'828)	<0.001	<0.001
Diabetes	31.6 (265/838)	29.0 (203/700)	17.2 (2'578/14'957)	0.29	<0.001
Dyslipidemia	67.5 (512/758)	66.9 (429/641)	57.7 (8'046/13'949)	0.82	<0.001
Smoking	20.3 (142/699)	28.2 (168/595)	45.4 (6'200/13'658)	0.001	<0.001
Obesity (BMI >30 kg/m^2)	22.9 (169/738)	23.1 (149/645)	20.5 (2'910/14'221)	0.95	0.03
Coronary artery disease	52.6 (439/834)	46.3 (321/693)	22.2 (3'370/15'174)	0.02	<0.001
Heart failure	11.0 (94/851)	4.4 (31/712)	1.8 (281/15'309)	<0.001	<0.001
Cerebrovascular disease	10.1 (86/851)	8.8 (63/712)	4.0 (608/15'359)	0.44	<0.001
Peripheral artery disease	9.5 (81/851)	7.4 (53/712)	3.6 (556/15'359)	0.15	<0.001
Kidney disease	21.0 (177/842)	15.0 (105/700)	4.9 (744/15'227)	<0.01	<0.001
Charlson comorbidity index >1	46.7 (393/842)	38.9 (272/700)	16.7 (2'531/15'176)	<0.01	<0.001

Table 1. Baseline characteristics of AMI patients according to initial ECG. BBB, bundle branch block; BMI, body mass index; LBBB, left bundle branch block; RBBB, right bundle branch block; STE, ST segment elevation.

Clinical presentation

Most patients presented with chest pain, particularly in the presence of AMI with STE (95% vs. 81% of the patients with LBBB or RBBB, $p<0.001$, **Table 2**). Half of the patients with LBBB had dyspnea, which was 22% and 46% less common in the presence of an RBBB or STE, respectively. Approximately 19% of patients with LBBB presented with pulmonary edema or cardiogenic shock, conditions that were 1.5- and 2.4-fold more frequent than in patients with RBBB and STE, respectively. Of the three groups of patients, individuals with LBBB also had the highest creatinine levels, and the longest hospital stays. In contrast, based on peak creatine kinase levels, infarct size was about 4-times larger if the initial ECG showed STE as compared with LBBB or RBBB. Of those patients who underwent coronary angiography (n=16'344, 94% of the patient cohort), about 40% with BBB had three-vessel coronary artery disease (vs. 25.3% of patients with STE, $p<0.001$, **Figure 1**), whereas patients with STE more frequently had single vessel coronary artery disease (42.7% vs. 28.1% and 24.8% of patients with RBBB or LBBB, respectively, $p<0.001$).

	LBBB (*n*=880)	RBBB (*n*=732)	STE (*n*=15'852)	*P* value (LBBB vs. RBBB)	*P* value (BBB vs. STE)
Chest pain, % (*n*/N)	81.3 (659/811)	81.5 (552/677)	95.4 (14'548/15'252)	0.95	<0.001
Dyspnea, % (*n*/N)	53.9 (416/772)	42.3 (265/627)	29.0 (3'914/13'502)	<0.001	<0.001
Systolic BP (mmHg), mean±SD	137±30	139±28	132±28	0.26	<0.001
Heart rate (bpm), mean±SD	86±24	82±22	79±19	<0.001	<0.001
Atrial fibrillation, % (*n*/N)	11.4 (100/880)	9.3 (68/732)	3.8 (598/15'839)	0.19	<0.001
Killip class ≥3, % (*n*/N)	18.8 (164/874)	12.0 (87/728)	7.9 (1'244/15'733)	<0.001	<0.001
Resuscitation prior to admission, % (*n*/N)	7.5 (66/880)	9.0 (66/732)	7.9 (1'257/15'842)	0.28	0.47
Patient delay (min), median (IQR)	230 (104, 719)	301 (116, 943)	165 (91, 370)	0.07	<0.001
Creatinine (μmol/L), median (IQR)	96 (78, 128)	93 (70, 116)	83 (70, 98)	<0.001	<0.001
Peak CK (IU/L), median (IQR)	346 (159, 816)	354 (171, 889)	1288 (497, 2'664)	0.06	<0.001
Hospital stay (days), median (IQR)	5 (2, 10)	5 (2, 9)	4 (2, 7)	0.02	<0.001

Table 2. Clinical presentation of AMI patients according to initial ECG. BBB, bundle branch block; BP, blood pressure; bpm, beats per minute; CK, creatine kinase; IQR, interquartile range; LBBB, left bundle branch block; RBBB, right bundle branch block; STE, ST segment

Hospital outcomes

The incidence of MACCE was highest in AMI patients with LBBB (13.9% vs. 9.9% and 6.7% in patients with RBBB and STE, respectively, $p<0.05$, **Table 3**), which was largely driven by the crude hospital mortality (12.8% vs. 8.9% and 5.6% in patients with RBBB and STE, respectively, $p<0.05$). Notable was also a ~2-fold higher incidence of cardiogenic shock developing during hospitalization in this patient population (7.6% vs. 3.9% and 3.8% in patients with RBBB and STE, respectively, $p<0.05$), whereas the incidence of reinfarction and stroke did not differ between groups. Acute renal failure was 2.4-times more common in patients with BBB (5.1% vs. 2.1% in patients with STE, $p<0.001$). After multivariate adjustment, hospital mortality was similar in the presence of an isolated LBBB compared to STE, while the presence of an isolated RBBB was associated with reduced mortality. In contrast, increased mortality was observed when an RBBB (but not LBBB) with concomitant STE was present in the initial ECG of AMI patients (OR 1.77, 95% CI 1.19-2.64, $p=0.005$ vs. STE, **Figure 2**). In the overall patient population, resuscitation prior to admission as well as presentation in Killip class ≥3 were most closely associated with hospital mortality. Increased mortality was also independently associated with a Charlson comorbidity index >1, increased age, heart rate and creatinine values, while higher systolic blood pressure and performance of PCI were associated with reduced mortality.

	LBBB (*n*=880)	RBBB (*n*=732)	STE (*n*=15'852)	*P* value (LBBB vs. RBBB)	*P* value (BBB vs. STE)
Primary outcome, % (*n*/N)					
MACCE	13.9 (121/871)	9.9 (71/720)	6.7 (1045/15'675)	0.02	<0.001
Secondary outcomes, % (*n*/N)					
Reinfarction	0.7 (6/871)	1.1 (8/720)	0.8 (127/15'675)	0.43	0.55
Stroke/TIA	0.9 (8/871)	1.3 (9/720)	0.7 (113/15'675)	0.63	0.09
Mortality	12.8 (113/880)	8.9 (65/732)	5.6 (885/15'852)	0.01	<0.001
Cardiogenic shock	7.6 (66/870)	3.9 (28/720)	3.8 (596/15'663)	<0.01	0.01
Acute renal failure	5.7 (50/871)	4.3 (31/720)	2.1 (328/15'666)	0.21	<0.001

Table 3. Primary and secondary hospital outcomes of AMI patients according to initial ECG. BBB, bundle branch block; LBBB, left bundle branch block; MACCE, major adverse cardiac and cerebrovascular events (a composite of reinfarction, stroke/TIA, and/or death); RBBB, right bundle branch block; STE, ST segment elevation; TIA, transient ischemic attack.

Therapy and outcomes in AMI patients undergoing primary PCI

The use of percutaneous coronary intervention (PCI) as the selected treatment strategy over the study period is shown in **Figure 3**. In all groups, the left anterior descending coronary artery was most frequently treated (~47% of patients, *p*=n.s. between groups). When compared to AMI patients with STE, more interventions to the left main (7.2% vs. 2.7%, *p*<0.001) and circumflex artery (31.4% vs. 18.2%, *p*<0.001) were performed in AMI patients with LBBB or RBBB, whereas the right coronary artery was less frequently treated (31.1% vs. 42.5%, *p*<0.001). Regarding the concomitant pharmacological therapy, antithrombotic medications were more likely to be administered to patients with STE, whereas diuretics and vasopressors were more frequently used in patients with LBBB (**Table 4**).

Crude hospital mortality was lower in patients subjected to a primary PCI strategy when compared to the overall cohort (**Tables 3 and 4**). However, MACCE and hospital mortality of AMI patients with BBB remained 1.9-fold (LBBB) and 1.8-fold (RBBB) higher compared to STE (MACCE: 9.5% vs. 9.1% vs. 5.5%, *p*<0.001 vs. STE; mortality: 8.6% vs. 8.1% vs. 4.5%, *p*<0.001 vs. STE, **Table 4**). Patients with LBBB had the highest incidence of cardiogenic shock (6.8% vs. 3.8% and 3.5% in patients with RBBB and STE, respectively, *p*<0.05).

	LBBB (*n*=524)	RBBB (*n*=484)	STE (*n*=14'401)	*P* value (LBBB vs. RBBB)	*P* value (BBB vs. STE)
Medical therapy, % (*n*/N)					
Aspirin	94.9 (488/514)	96.0 (455/474)	98.0 (13'927/14'204)	0.45	<0.001
$P2Y_{12}$ inhibitor	89.7 (462/515)	90.3 (427/473)	96.2 (13'657/14'203)	0.83	<0.001
Heparin	84.2 (433/514)	82.8 (391/472)	92.3 (13'079/14'173)	0.61	<0.001
GPIIb/IIIa inhibitor	7.9 (40/506)	9.5 (44/463)	24.3 (3'402/14'015)	0.42	<0.001
Nitrate	41.4 (210/507)	45.9 (214/466)	46.8 (6'564/14'026)	0.17	0.17
Statin	69.5 (356/512)	75.5 (357/473)	79.0 (11'163/14'129)	0.04	<0.001
Diuretic	39.7(202/509)	28.5 (133/467)	14.3 (2'001/14'022)	<0.001	<0.001
Betablocker	51.6 (264/512)	53.1 (250/471)	53.8 (7'587/14'092)	0.66	0.46
ACE-I/ARB	55.6 (285/513)	55.5 (261/470)	60.1 (8'499/14'131)	1.00	<0.01
Calcium channel blocker	16.2 (82/505)	17.5 (82/468)	10.7 (1'494/13'982)	0.61	<0.001
Vasopressor	15.0 (76/507)	10.5 (49/466)	11.1 (1'557/14'004)	0.04	0.41
Primary outcome, % (*n*/N)					
MACCE	9.5 (49/517)	9.1 (43/475)	5.5 (789/14'249)	0.83	<0.001
Secondary outcomes, % (*n*/N)					
Reinfarction	0.6 (3/517)	0.8 (4/475)	0.8 (114/14'249)	0.72	0.88
Stroke/TIA	1.2 (6/517)	0.8 (4/475)	0.7 (99/14'249)	0.76	0.38
Mortality	8.6 (45/524)	8.1 (39/484)	4.5 (643/14'401)	0.82	<0.001
Cardiogenic shock	6.8 (35/516)	3.8 (18/475)	3.5 (495/14'239)	0.04	0.04
Acute renal failure	5.2 (27/517)	4.2 (20/475)	2.0 (286/14'242)	0.55	<0.001

Table 4. Hospital therapy and outcomes of AMI patients subjected to primary PCI according to initial ECG. ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin AT_1 receptor blocker; BBB, bundle branch block; LBBB, left bundle branch block; MACCE, major adverse cardiac and cerebrovascular events (a composite of reinfarction, stroke/TIA, and/or death); RBBB, right bundle branch block; STE, ST segment elevation; TIA, transient ischemic attack.

Discussion

In this large prospective cohort of unselected patients admitted with AMI, we found that the presence of a new or presumably new BBB in the ECG at presentation was associated with a higher prevalence of preexisting cardiovascular disease, high-risk clinical features, multivessel disease, and with worse unadjusted outcomes when compared to isolated STE. This finding was more pronounced in the presence of an LBBB than an RBBB. After multivariate adjustment, mortality in the presence of an isolated LBBB was similar compared to STE, while an isolated RBBB was associated with reduced mortality. Increased hospital mortality was only observed when an RBBB with concomitant STE was present. This suggests that the presence of an isolated LBBB or RBBB reflects the patient's higher baseline cardiovascular risk rather than independently contributing to adverse clinical outcomes in AMI.

The presence of a BBB in AMI patients has previously been associated with abundant comorbidities and a high incidence of cardiogenic shock.[4-13, 15-17, 24] We extend these findings demonstrating substantial, clinically relevant differences between the BBB types. Indeed, individuals with an LBBB were older, more likely to be female, and more frequently had a history of preexisting cardiovascular disease and acute heart failure on admission compared to patients with an RBBB. Given that more high-risk characteristics are present in AMI patients with an LBBB compared with an RBBB (and even more compared with isolated STE), the worse unadjusted outcomes may not be surprising. Indeed, older age as observed in patients with LBBB is strongly related not only to fibrotic changes in the conduction system leading to BBBs, but also potentially underlying chronic ischemic and non-ischemic conditions, including left ventricular hypertrophy and remodeling (most commonly resulting from long-standing hypertension) as well as valvular heart disease.[3]

Moreover, because it is often not possible to determine the chronicity of BBBs due to lack of a recent ECG before the development of an AMI, many BBBs considered presumably new may not result from acute myocardial ischemia, but rather reflect underlying structural heart disease that, in turn, increases the risk for adverse outcomes in AMI. Thus, the higher unadjusted mortality in AMI patients with an LBBB compared to patients with an RBBB (and even more compared with isolated STE) may be largely explained by preexisting cardiac pathologies serving as a substrate for conduction abnormalities.[3] In line with this notion, we have previously shown that only clinical factors such as the Killip class and a history of heart failure, but no specific ECG changes, have critical discriminative performance in predicting hospital mortality among the AMIS-Plus cohort.[25]

The current evidence has been conflicting regarding the independent prognostic value of an LBBB or RBBB in AMI patients.[4, 6, 8-17, 24] However, this may be due to the small sample size in some registries,[5, 13-16] while others date back to the fibrinolytic era not considering current treatment strategies, PCI in particular.[4, 6, 8, 10, 16, 24] We report on the clinical significance of BBBs in a large contemporary prospective cohort of unselected AMI patients, with a high proportion treated with primary PCI reflecting the recommended strategy in current guidelines.[1, 2] However, as with previous studies on patients undergoing an invasive therapeutic strategy,[9, 14] the decision to intervene was left at the discretion of the treating physicians. The lower unadjusted mortality in the subset of AMI patients with LBBB or RBBB undergoing primary PCI may thus be confounded by a selection bias. Nevertheless, patients with BBBs still had worse outcomes compared to STE despite invasive therapy, supporting the concept of this being a risk marker reflecting preexisting heart disease. In addition, although the degree of myocardial damage may be related to the development of BBBs, they were associated with a 4-fold smaller infarct size compared to isolated STE as assessed by peak creatine kinase levels, suggesting (i) that infarct size does

not explain the worse clinical outcomes and (ii) that an occluded culprit artery was likely often not found when STE was absent.

We would like to highlight that true AMI-related new BBBs carry a very high mortality risk, but may be challenging to recognize.[1-3, 9] Our finding that an RBBB with concomitant STE was independently associated with increased hospital mortality compared to isolated STE is in line with previous observations[9, 14] that such patients have a very high likelihood of an occluded culprit artery warranting urgent revascularization. Likewise, an RBBB was shown to predict mortality in STEMI, but not in NSTEMI patients,[24] because it usually reflects a large anterior AMI involving the right bundle transversing the intraventricular septum typically due to occlusion of the proximal left anterior descending artery.[3, 6] The presence of STE may be more difficult to recognize in the presence of an LBBB compared with an RBBB because of more pronounced ST-segment abnormalities.[1, 2] With the exception of STE concordance, current ECG algorithms are complex and have limited specificity, which may partly explain why an LBBB with concomitant STE had similar hospital mortality compared with isolated STE in our study.[1-3, 26]

The present study has certain limitations. As with all registries, even when data were collected prospectively, drawing conclusions on clinical outcomes needs to be done cautiously, because the revealed associations may not reflect actual causal links. We thus cannot comment on current recommendations to treat an AMI with (presumably) new isolated LBBB[1, 2] or RBBB[2] as a STEMI equivalent and, hence, it remains to be determined in future studies which of these very high risk patients benefit most from an early invasive strategy. On the other hand, randomized clinical trials often do not adequately represent patients with extensive comorbidities or at high age,[27] which represents the typical population when studying AMI with BBBs. Furthermore, our large population-based dataset more likely reflects routine clinical practice,[27] where

many patients presenting with AMI do not have a previous ECG for comparison. Of note, ECG verification by a core laboratory is not performed in the AMIS-Plus registry, and we did not discriminate whether a new LBBB or RBBB was transient or permanent, with only the latter being an independent predictor of mortality.[7, 10] Furthermore, we report on implications that the presence of BBBs in AMI patients has on hospital outcomes but not on intermediate or long-term follow-up.

In conclusion, an isolated BBB in patients with AMI is associated with extensive comorbidities, high-risk clinical features and worse unadjusted outcomes compared to isolated STE. However, this appears to be largely explained by underlying heart disease as a substrate for conduction abnormalities,[3] rather than the BBB itself. Independently increased mortality was only observed with true AMI-related RBBB characterized by concomitant STE, which likely represent the patients who benefit most from urgent revascularization therapy.

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Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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Figure Legends

Figure 1. Severity of coronary artery disease according to initial ECG. AMI, acute myocardial infarction; LBBB, left bundle branch block (*n*=673); RBBB, right bundle branch block (*n*=597); STE, ST segment elevation (*n*=15'074).

Figure 2. Clinical variables independently associated with hospital mortality. Odds ratios have been calculated using AMI patients with isolated STE as reference. bpm, beats per minute; CI, confidence interval; LBBB, left bundle branch block; RBBB, right bundle branch block; STE, ST segment elevation.

Figure 3. Temporal trends in PCI performed in patients with AMI and isolated LBBB, RBBB or STE. AMI, acute myocardial infarction; LBBB, left bundle branch block; RBBB, right bundle branch block; STE, ST segment elevation.